UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

Office of Chemical Safety and Pollution Prevention

MEMORANDUM

Date: August 8, 2018

SUBJECT: Common Triazole Metabolites: Updated Aggregate Human Health Risk Assessment to Address New Section 3 Registrations For Use of Prothioconazole and Tebuconazole.

PC Codes: 600074 (1,2,4-Triazole), 600011 (Triazolylalanine), 600082 (Triazolylacetic Acid)	DP Barcode: D448162
Decision No: 537553	Registration No.: None
Petition No.: 7E8648	Regulatory Action: Section 3
Assessment Type: Single Chemical, Aggregate	Registration Case No.: NA
TXR No.: None	CAS No.: 288-88-0, 86362-20-1
MRID No.: None	40 CFR: None

From: Thurston G. Morton, Senior Chemist
Risk Assessment Branch IV
Health Effects Division (HED) 7509P

Through: Donald Wilbur, Branch Chief
Risk Assessment Branch IV
Health Effects Division (HED) 7509P

To: Lata Venkateshwara
Minor Use and Emergency Response Branch
Registration Division (7505P)

I. CONCLUSIONS

Based on conservative, health-protective assumptions, aggregate risk estimates associated with 1,2,4-triazole (T) and the conjugated triazole metabolites [i.e., combined residues of triazolylalanine (TA), and triazolylacetic acid (TAA)] are below HED's level of concern. There are no human heath risk issues for these metabolites that would preclude the requested uses of prothioconazole and tebuconazole.

II. ACTION REQUESTED

Update the aggregate human health risk assessments for T and the conjugated triazole metabolites to account for the new uses of prothioconazole and tebuconazole.

III. BACKGROUND

In 2006, HED issued aggregate human health risk assessments for T and the conjugated triazole metabolites (M. Doherty, *et al*., D322215, 02/07/2006). Those assessments addressed a back-log of triazole use requests that had been held by the Agency pending resolution of various toxicological and exposure concerns for the common triazole metabolites. The findings of that assessment were that risk estimates for all exposure scenarios were below HED's level of concern. Since that time, a number of requests for new uses of triazole-derivative fungicides have been submitted to the Agency. As a result of these requests, new dietary exposure estimates have been made for T and combined residues of TA, and TAA, and new aggregate exposure and risk estimates are necessary. Neither the toxicological information nor the non-dietary exposure estimates detailed in the 2006 memorandum have changed; thus the only alterations to the previous aggregate exposure and risk estimates are due to changes in the dietary exposure estimates. For complete hazard characterization and non-dietary exposure assessments for the common triazole metabolites, see the 2006 risk assessment.

IV. RESULTS/DISCUSSION

As noted above, the only revisions to the components of the previous aggregate exposure and risk estimates are to the dietary exposure estimates. For the common triazole metabolites, acute and chronic aggregate risks consist only of dietary (food + water) components and, therefore, are equivalent to the dietary risk estimates provided in the most recent dietary exposure assessment (T. Morton, D448161, 08/08/2018).

The revised aggregate estimates are summarized below for short- and intermediate-term scenarios for T (Tables 2 and 3, respectively). The conjugated triazole metabolites are formed in plants by the conjugation of 1,2,4-T to serine. The TA may then be further metabolized to form TAA. Because of the nature of this process, HED has assumed that it occurs within the plant itself and not on leaf surfaces. Therefore, the residues are not available for dermal, hand-to-mouth, or object-to-mouth exposures and HED has not conducted a residential exposure assessment for the triazole conjugates. Residues of TA and TAA may occur in soil. 1,2,4-Triazole is more toxic than TA/TAA and exposures to these via soil ingestion are unlikely to exceed those of 1,2,4-T. The assessment for soil ingestion of 1,2,4-T shows that risk estimates are below HED's level of concern; therefore, risk estimates for soil ingestion of the conjugates will also be below HED's level of concern.

Table 1. Summary of Dietary (Food and Drinking Water) Exposure and Risk for the Common Triazole Metabolites Adding the New Uses for Prothioconazole and Tebuconazole.						
Population Subgroup	Acute Dietary (95th Percentile)		Chronic Dietary		Cancer	
	Dietary Exposure (mg/kg/day)	% aPAD*	Dietary Exposure (mg/kg/day)	% cPAD*	Dietary Exposure (mg/kg/day)	Risk
1,2,4-Triazole						
General U.S. Population	0.008447	28	0.001199	24	Not Applicable	Not Applicable
All Infants (< 1 year old)	0.012849	43	0.002049	41		
Children 1-2 years old	**0.023416**	**78**	**0.003783**	**76**		
Children 3-5 years old	0.019033	63	0.002886	58		
Children 6-12 years old	0.011174	37	0.001532	31		
Youth 13-19 years old	0.007231	24	0.000960	19		
Adults 20-49 years old	0.006595	22	0.000997	20		
Adults 50-99 years old	0.005772	19	0.000945	19		
Females 13-49 years old	0.006745	22	0.000971	19		
Triazolylalanine + Triazolylacetic Acid						
General U.S. Population	Not Applicable	Not Applicable	0.016626	19	Not Applicable	Not Applicable
All Infants (< 1 year old)			0.024637	27		
Children 1-2 years old			**0.058226**	**65**		
Children 3-5 years old			0.044620	50		
Children 6-12 years old			0.022959	26		
Youth 13-19 years old			0.013744	15		
Adults 20-49 years old			0.013141	15		
Adults 50-99 years old			0.012376	14		
Females 13-49 years old	**0.078251**	**78**	0.012764	14		

* The values for the highest exposed population for each type of risk assessment are bolded.

Table 2. Short-term Aggregate Exposure and Risk Estimates for 1,2,4-Triazole.								
	Exposure Estimate, mg/kg/day[1]							
Population Subgroup	Dietary	Dermal (M/L/A)	Dermal (Post-Applic.)	Hand-to-Mouth	Object-to-Mouth	Soil Ingestion	Aggregate	Aggregate MOE[2]
U.S. Population (total)	0.001199	0.00183	0.0051	N/A	N/A	N/A	0.008129	3700
All infants (< 1 year)	0.002049	N/A	0.0086	0.0041	0.0010	0.000019	0.015768	1900
Children 1-2 yrs	**0.003783**	N/A	0.0086	0.0041	0.0010	0.000019	0.017502	1700
Children 3-5 yrs	0.002886	N/A	0.0086	0.0041	0.0010	0.000019	0.016605	1800
Children 6-12 yrs	0.001532	N/A	0.0086	N/A	N/A	N/A	0.010132	3000
Youth 13-19 yrs	0.000960	0.00183	0.0051	N/A	N/A	N/A	0.00789	3800
Adults 20-49 yrs	0.000997	0.00183	0.0051	N/A	N/A	N/A	0.007927	3800
Adults 50-99 yrs	0.000945	0.00183	0.0051	N/A	N/A	N/A	0.007875	3800
Females 13-49 yrs	0.000971	0.00183	0.0051	N/A	N/A	N/A	0.007901	3800

[1] Exposure estimates for dermal, hand-to-mouth, object-to-mouth, and soil ingestion are from J. Arthur, DP 322240, 12/9/05.
[2] Aggregate MOE = NOAEL (30 mg/kg/day) ÷ Aggregate Exposure Estimate (mg/kg/day). Level of Concern = 1000.

Table 3. Intermediate-term Aggregate Exposure and Risk Estimates for 1,2,4-Triazole.				
	Exposure Estimate, mg/kg/day			
Population Subgroup	Dietary	Soil Ingestion[1]	Aggregate	Aggregate MOE[2]
U.S. Population (total)	0.001199	N/A	0.001199	13000
All infants (< 1 year)	0.002049	0.000019	0.002068	7300
Children 1-2 yrs	**0.003783**	0.000019	0.003802	3900
Children 3-5 yrs	0.002886	0.000019	0.002905	5200
Children 6-12 yrs	0.001532	N/A	0.001532	9800
Youth 13-19 yrs	0.000960	N/A	0.00096	16000
Adults 20-49 yrs	0.000997	N/A	0.000997	15000
Adults 50-99 yrs	0.000945	N/A	0.000945	16000
Females 13-49 yrs	0.000971	N/A	0.000971	15000

[1] Soil ingestion estimates are from J. Arthur, DP 322240, 12/9/05

[2] Aggregate MOE = NOAEL (15 mg/kg/day) ÷ Aggregate Exposure Estimate (mg/kg/day). Level of Concern = 3000.